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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/512,701	02/25/2000	JOHN P. LEONARD	GI5229FWC-DIV1	7087

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EXAMINER	
MINNIFIELD, NITA M	
ART UNIT	PAPER NUMBER
1645	17

DATE MAILED: 07/16/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Offic Action Summary	Application N .	Applicant(s)	
	09/512,701	LEONARD ET AL.	
	Examiner	Art Unit	
	N. M. Minnifield	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 April 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *16-31* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *16-31* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Response to Amendment

1. Applicants' amendment filed April 29, 2002 is acknowledged and has been entered. New claims 21-31 have been added. Claims 16-31 are now pending in the present application. All rejections have been withdrawn in view of Applicants' amendment with the exception of those discussed.

2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

3. Claims 16-29 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gately et al (5650492) taken with Trinchieri et al (1992).

Gately et al teach "IL-12 p 40 homodimer is useful as an IL-12 antagonist to block activity of IL-12 in pathologic immune responses. Current evidence from both in vitro and in vivo studies suggest that Il-12 plays an important role in the development of Th1-type helper T cells which promote cell-mediated immune responses, in triggering gamma interferon production by mature T and/or NK cells and in facilitating specific cytolytic T lymphocyte responses. Excessive activity of Th1 cells and/or excessive production of gamma interferon may be involved in the pathogenesis of some autoimmune disorders and septic shock, indicating that IL-12 p40 homodimer should be useful in the treatment of disorders such as rheumatoid and other inflammatory arthtidies, Type I diabetes mellitus, multiple sclerosis, systemic lupus erythematosus, septic shock, etc." (cols. 3-4). Gately et al teaches that IL-12 was formerly known as cytotoxic lymphocyte maturation factor or natural killer cell stimulatory factor (col. 1). Gately et al teaches that IL-12 is a heterodimeric molecule with a molecular weight of 75 kDa consisting of two subunits, 35 kDa (p35) and 40 kDa (p40) (col. 1). "Studies with neutralizing antibodies to human IL-12

and site-specific chemical modification suggested that the p40 subunit contains epitopes important for IL-12 binding to its receptor." (col. 1). Gately et al teaches that the dose ranges may be determined by those of ordinary skill in the art without undue experimentation as well different modes of administration (parenterally, intraperitoneally, intramuscularly, subcutaneously) (col. 4). The prior art discusses the use of IL-12 antagonists in the treatment of conditions promoted by an increase of interferon gamma, but does not specifically mention the IL-12 antagonist being an antibody immunoreactive to IL-12.

However, Trinchieri et al teach that IL-12 is needed for optimal IFN gamma production (p. 355; 362). "Importantly, a mixture of anti-NKSF/IL-12 and anti-TNF antibodies almost completely suppressed IFN-gamma production to levels comparable to those obtained with IL-10." (p. 363). Therefore it would have been obvious to a person of ordinary skill in the art at the time of the invention to use the teachings of the prior art as set forth above with the expected benefit of developing a method of using an IL-12 antagonist (anti-IL-12) to decrease the production of interferon gamma to prevent or treat autoimmune conditions in humans, since the art teaches that an increase in interferon gamma is involved in the pathogenesis of autoimmune diseases.

Further, as asserted by Applicants in the response (6/15/01), that rheumatoid arthritis is an autoimmune condition promoted by an increase in levels of interferon-gamma and/or TNF-alpha and that IL-12 is known to induce TNF-alpha and IFN-gamma, therefore the skilled artisan would have no reason to doubt that an antagonist to IL-12 would be useful in the treatment in the rheumatoid arthritis.

Since the art teaches the concept that a block in the production of IFN-gamma production would be a means/therapy for the treatment of RA for example (a disease whose pathology is considered to be caused by an increase in IFN-gamma) and that IL-12 induces IFN-gamma, it would have been obvious to a person

of ordinary skill in the art at the time of the invention to use the teachings of the prior art as set forth above with the expected benefit of developing a method of using an IL-12 antagonist (anti-IL-12), to block IL-12 which in turn decreases the production of IFN-gamma to treat RA in humans or any other condition that is promoted by an increase in levels of IFN-gamma. It would have been obvious to a person of ordinary skill in the art at the time the invention was made to use a composition that would block or hinder IFN-gamma production since the art teaches that IFN-gamma is involved in autoimmune diseases. Blocking the production of IFN-gamma by using an IL-12 antagonist, would have been a reasonable method for the treatment of RA. The claimed invention is prima facie obvious in view of the prior art absent any convincing evidence to the contrary.

4. Claims 23, 24, 30 and 31 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for using an IL-12 antibody, does not reasonably provide enablement for use of an antibody binds to a 40 kD or 35 kD subunit of IL-12. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims. The specification has not taught such an antibody that only binds to the 40 kD or 35 kD subunit of the IL-12 and will still be able to treat rheumatoid arthritis in a human. Further, the specification is not enabled for the scope of claims 30 and 31, which are directed, methods of treating rheumatoid arthritis by administering IL-12 antagonists in combination with other therapies for autoimmune conditions; therapies comprise steroidal or other anti-inflammatory therapies.

5. No claims are allowed.

6. Any inquiry concerning this communication or earlier communications from the examiner should be directed to N. M. Minnifield whose telephone number is 703-305-3394. The examiner can normally be reached on M-F (8:00-5:30) Second Friday Off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette R.F. Smith can be reached on 703-308-3909. The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-4556 for regular communications and 703-308-4556 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

N. M. Minnifield
Primary Examiner
Art Unit 1645

nmm

July 15, 2002